

Glioblastoma in the Cerebellopontine Angle in a Patient with Neurofibromatosis Type I: A Case Report and Review of the Literature

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Abstract

Keywords

- cerebellopontine angle
- neurofibromatosis type I
- glioblastoma multiforme

Introduction Glioblastoma multiforme (GBM) is the most common primary brain malignancy in adults and is typically in the supratentorial cerebral hemispheres. It has been reported to occur in the posterior fossa at the cerebellopontine angle (CPA), but the incidence is extremely rare.

Case Report We report a case of a patient with a history of neurofibromatosis type I (NFI) diagnosed with a GBM arising in the CPA after presenting with facial numbness and pain. Patients with NFI are known to have an increased risk of developing both benign and malignant tumors, including a propensity for brainstem gliomas. However, there is no known association between NFI and tumors of the CPA. We believe this is the first reported case of a GBM of the CPA in a patient with NFI.

Conclusion Although rare, GBM should be included in the differential diagnosis of a patient with a CPA tumor, especially in patients with increased risk of malignant pathology.

Introduction

Glioblastoma multiforme (GBM) is the most common primary brain tumor in adults, comprising 15 to 20% of all intracranial tumors.^{1–3} They usually present in the supratentorial region within the cerebral hemispheres. Posterior fossa or cerebellopontine angle (CPA) occurrence is unusual and may pose a clinical challenge as it may mimic other, more commonly seen neoplasms in this location.^{4,5} Within the CPA, they typically arise intra-axially from the cerebellum or pons with lateral exophytic extension.^{4–11} Internal auditory canal (IAC) involvement is rare, with very few cases reported in the literature.^{3,5,12} There is no documented association between CPA glioblastomas and genetic or syndromic disorders. We present a case of a 48-year-old patient with neurofibromatosis type I (NFI) with an intra-axial GBM arising within the CPA.

Case Report

Clinicoradiographic Presentation

A 48-year-old male patient presented with a 1-month history of progressive right-sided facial numbness and pain. He denied any other neurologic symptoms. His past medical and surgical history were significant for NFI, chronic vocal cord paralysis secondary to numerous procedures in childhood to excise laryngeal neurofibromas, and a Whipple procedure for pancreatic ampullary carcinoma.

Physical examination demonstrated right facial hypesthesia, but all other cranial nerves were intact. An audiogram was obtained with normal hearing bilaterally.

Magnetic resonance imaging (MRI) of the brain and brainstem revealed a right heterogeneous T1 hypointense, T2 hyperintense contrast-enhancing 3.7 cm intra-axial mass with central necrosis centered within the right ventral pons

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with extension superiorly to the midbrain. Additionally, there was an 8-mm satellite lesion in the anteromedial paramedian pons (►Fig. 1). There was surrounding regional mass effect with partial effacement of the right fourth ventricle and midline shift at the level of the midsuperior pons with no IAC involvement.

Surgical Approach

The patient underwent a combined transpetrosal-retroigmoid approach, and the tumor had an ill-defined plane separating it from the cerebellum and adjacent pons. Frozen section histopathology showed poorly differentiated malignant neoplasm with focal rhabdoid features, suggesting a tumor of glial origin. The patient underwent a subtotal tumor resection due to the dangerous medial plane of dissection.

Postoperative Course

The patient's postoperative course was uncomplicated, and he was discharged on postoperative day 3. The final pathology revealed this to be a diffuse, high-grade astrocytoma, and WHO grade IV. Immunohistochemical stains showed glial fibrillary acidic protein positivity, consistent with glioblastoma.¹³ The IDH1 mutant was negative. After his scheduled visits with hematology and radiation oncology, protocol-based therapy for GBM was initiated and he began temozolomide with planned concurrent radiation therapy.

Discussion

Cerebellopontine angle tumors are the most common neoplasms in the posterior fossa and may be classified based on their site of origin as either intra-axial or extra-axial.^{14,15} Although the majority of tumors that arise in this location are

benign, more sinister entities may occur. Only 11 cases of primary glioblastoma have been reported in the CPA (►Table 1). Most of these tumors have an intra-axial site of origin within the cerebellum or pons and appear to exhibit secondary exophytic extension into the CPA.⁴⁻¹¹ Only three of the described lesions involved the IAC.^{3,5,12} None of the patients in the literature had syndromic or genetic predispositions that contributed to tumorigenesis.

Based on the current literature, we report the first case of primary CPA GBM arising from two distinct foci in a patient with NFI. This is an autosomal dominant genetic disorder due to mutations in the NFI, tumor-suppressor gene on chromosome 17, which results in loss of or reduced function of the protein neurofibromin.^{16,17} Ultimately, this is responsible for a wide spectrum of clinical manifestations ranging from café-au-lait macules to central nervous system tumors causing neurologic complications.¹⁸ Despite no previously documented association between this genetic syndrome and CPA GBM, it is known that there are thousands of distinct and unique pathogenic mutations in affected patients with NFI. Correlations between genotype and phenotype in patients with NF1 are more difficult to predict in patients with smaller mutations (<20 base pairs) in the NFI gene.¹⁹ It is known, however, that a mutation in the NFI gene places patients at increased risk to develop both benign and malignant tumors throughout their lifetime.^{20,21} More specifically, they have an increased propensity to develop gliomas in the brainstem.^{16,22} Independent risk factors associated with mortality and tumor aggressiveness in this cohort include symptomatic tumors, extra-optic location, and adult patients.²²

Our patient's neoplasm manifested acutely with a complete, right-sided trigeminal sensory deficit. Based on our imaging findings and, specifically, the lack of IAC involvement,

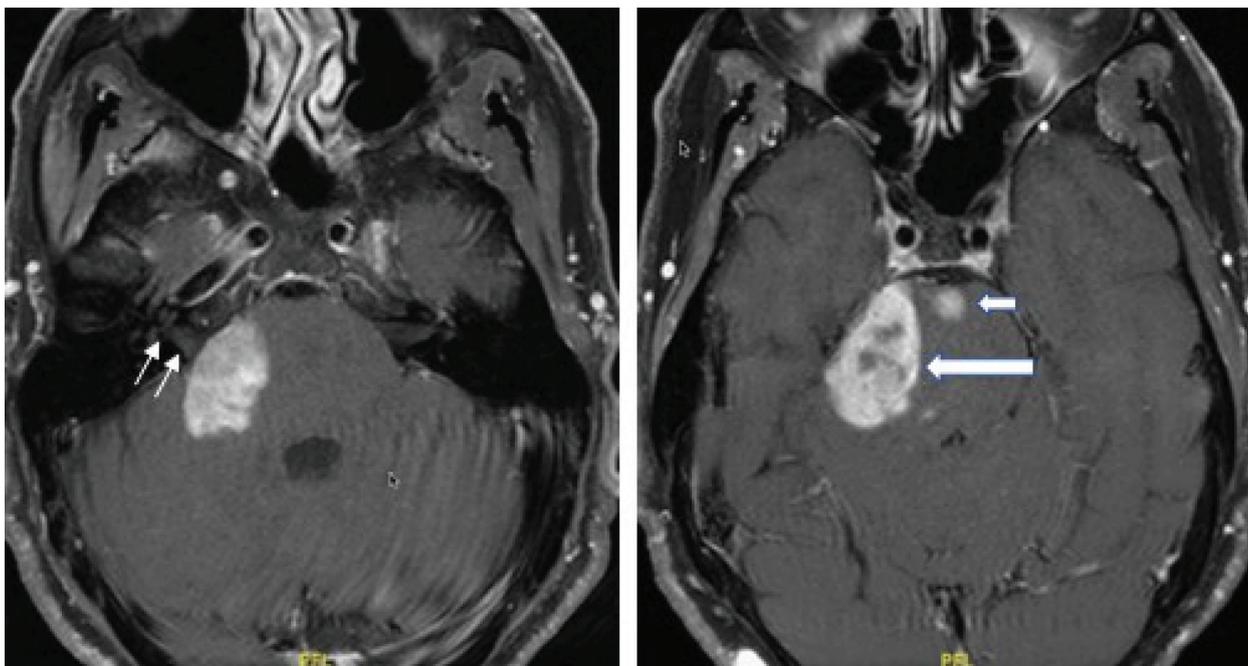


Fig. 1 Axial T1 weighted contrast enhancing lesions in the right cerebellopontine angle (long white arrow) without internal auditory canal involvement (double arrow) and ventral brainstem (short white arrow).

Table 1 Summary of cerebellopontine angle glioblastoma case reports

Authors	Sex/Age (y)	Site of origin	IAC involvement	Symptom duration	Treatment	Prognosis
Swaroop and Whittle ⁵	M/22	Pons	Yes	12 months	Subtotal resection	Unknown
Kasliwal et al ⁷	M/11	Cerebellum	No	15 days	Subtotal resection	Died after 2 months
Rasalingam et al ¹⁰	M/9	Pons	No	2 weeks	Subtotal resection	Alive after 2 months
Wu et al ³	M/60	CN VIII	Yes	2 months	Subtotal resection	Died after 2 months
Salunke et al ¹¹	M/59	Pons	No	3 months	Subtotal resection and RT	Unknown
Matsuda et al ⁹	M/69	Cerebellum	No	1 hour	Subtotal resection with chemotherapy and RT	Alive after 24 months
Lee et al ⁸	F/71	Cerebellum	No	3 months	Stereotactic biopsy with chemotherapy and RT	Alive after 12 months
Panigrahi et al ⁴	F/52	Possible cerebellum	No	2 months	Subtotal resection and RT	Alive after 3 months
Chen et al ⁶	F/5	Pons	No	5 months	Subtotal resection	Died after 2 months
Yang et al ¹	M/55	CN VIII	No	3 months	Subtotal resection	Died after 2.5 months
Takami et al ¹²	M/55	Possible CN VIII	Yes	19 months	Subtotal resection and RT	Alive after 5 months
Present case	M/48	Pons	No	1 month	Subtotal resection, RT, and chemotherapy	Alive after 3 months

Abbreviations: CN, cranial nerve; F, female; IAC, internal auditory canal; M, male; RT, radiation therapy.

a vestibular schwannoma was unlikely. The formulated differential diagnosis included trigeminal schwannoma, meningioma, primary brain malignancy, or metastatic disease. Due to the complexity of our patient's clinical characteristics, a diagnosis was only established after histopathological studies were finalized.

As with the other reported cases of CPA GBM, our patient's clinical characteristics made preoperative diagnosis difficult as the tumor mimicked more benign and commonplace lesions that typically arise within that site. In terms of management, the postoperative ramifications that accompanied the diagnosis were significant. Treatment for GBM follows a triple-based protocol regimen involving gross tumor resection, chemotherapy, classically with the alkylating drug temozolomide, and concurrent radiotherapy.^{2,9} Despite this aggressive approach to treatment, prognosis of GBM is dismal, with most patients only surviving 1 year after the initial diagnosis.²³ This is in stark contrast to CPA schwannomas, which can be managed with radiographic surveillance, radiotherapy, or surgical resection.^{24,25} After his initial hematology-oncology evaluation, our patient was started on 140 mg of temozolomide daily with a plan to initiate RT. Long-term prognosis for CPA GBM is not well described and is based on a limited number of anecdotal case reports. It is worth noting that longer survival was observed in the patients receiving all three therapeutic options concurrently.^{8,9}

In conclusion, we provided a case of primary intra-axial CPA GBM mimicking a more benign entity in a patient with

NFI with the intention of providing insight into the clinicoradiographic presentation and natural history of this tumor. Although rare, GBM should be considered in the differential diagnosis, especially if the clinical course is rapid and progressive with multifocal brain involvement. Special attention should be directed to patients with NF1, as they have a higher likelihood of presenting with rare and more aggressive pathology.

Note

This work will be presented as a poster at the North American Skull Base Society annual meeting in February 2020. This manuscript has not previously been published and is not under consideration by another journal at this time.

Conflict of Interest

None declared.

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